

CLAIMS

1. DNA sequence which encodes a protein of interest which contains regions having a high content of codons which are poorly suited to yeasts, characterized in that a sufficient number of codons which are poorly suited to yeasts is replaced with corresponding codons which are well-suited to yeasts in the said regions having a high content of codons which are poorly suited to yeasts.

2. Sequence according to claim 1, characterized in that the codons which are poorly suited to yeasts are selected from among codons whose frequency of use by yeasts is less than or equal to approximately 13 per 1000, preferably less than or equal to approximately 12 per 1000, more preferably less than or equal to approximately 10 per 1000.

3. Sequence according to claim 2, characterized in that the codons which are poorly suited to yeasts are selected from among codons CTC, CTG and CTT, which encode leucine, codons CGG, CGC, CGA, CGT and AGG, which encode arginine, codons GCG and GCC, which encode alanine, codons GGG, GGC and GGA, which encode glycine, and codons CCG and CCC, which encode proline.

4. Sequence according to claim 3, characterized in that the codons which are poorly suited to yeasts are selected from among codons CTC and CTG, which encode leucine, codons CGG, CGC, CGA, CGT

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and AGG, which encode arginine, codons GCG and GCC, which encode alanine, codons GGG and GGC, which encode glycine, and codons CCG and CCC, which encode proline.

5. ~~Sequence according to one of claims 1 to~~  
5 *Claims 1* ~~4~~, characterized in that the corresponding codons which are well-suited to yeasts are selected from among codons which correspond to the codons which are poorly suited to yeasts and which encode the same amino acids, and whose frequency of use by yeasts is greater than 15  
10 per 1000, preferably greater than or equal to 18 per 1000, more preferably greater than or equal to 20 per 1000.

6. Sequence according to claim 5,  
characterized in that the corresponding codons which  
15 are well-suited to yeasts are selected from among codons TTG and TTA, preferably TTG, which encode leucine, codon AGA, which encodes arginine, codons GCT and GCA, preferably GCT, which encode alanine, codon GGT, which encodes glycine, and codon CCA, which  
20 encodes proline.

7. ~~Sequence according to one of claims 1 to~~  
7 *Claim 1* ~~4~~, characterized in that the regions having a high content of codons which are poorly suited to yeasts contain at least 2 poorly suited codons among 10  
25 consecutive codons, with it being possible for the two codons to be adjacent or separated by up to 8 other codons.

8. Sequence according to claim 7,

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characterized in that the regions having a high content of poorly suited codons contain 2, 3, 4, 5 or 6 poorly suited codons per 10 consecutive codons, or contain at least 2 or 3 adjacent poorly suited codons.

5 9. DNA, in particular cDNA, sequence which encodes a protein of interest which contains regions having a high content of leucine, characterized in that a sufficient number of CTC codons encoding leucine in the said region having a high content of leucine is  
10 replaced with TTG and/or TTA codons, or in that a sufficient number of CTC and CTG codons encoding leucine in the said region having a high content of leucine is replaced with TTG and/or TTA codons.

10. Sequence according to claim 9,  
15 characterized in that the CTC or CTC and CTG codons are replaced with a TTG codon.

*Claim 9*  
20 11. Sequence according to ~~one of claims 9 or 10~~, characterized in that the regions having a high content of leucine contain 2, 3, 4, 5 or 6 leucines per 10 consecutive amino acids, or contain at least 2 or 3 adjacent leucines.

*Claim 1*  
25 12. Sequence according to ~~one of claims 1 to 11~~, characterized in that the general content of poorly suited codons is at least 20%, more preferably at least 30%, as compared with the total number of codons.

*Claim 1*  
13. Sequence according to ~~one of claims 1 to 12~~, characterized in that it contains at least one 5' region having a high content of codons which are poorly

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suited to yeasts.

14. Sequence according to claim 13, characterized in that the codons which are poorly suited to yeasts are replaced only in this 5' region.

5 ~~Claim 1~~ 15. Sequence according to ~~one of claims 1 to 14~~, characterized in that it is an isolated DNA sequence of natural origin, in particular of plant origin.

10 16. Sequence according to claim 15, characterized in that it originates from dicotyledonous or monocotyledonous plants, in particular from monocotyledonous plants.

15 17. Sequence according to claim 16, characterized in that it originates from plants of the gramineae family, which are selected, in particular, from among wheat, barley, oats, rice, maize, sorghum and cane sugar.

18. Sequence according to ~~one of claims 1 to 17~~, characterized in that it encodes an enzyme.

20 19. Sequence according to claim 18, characterized in that it encodes a cytochrome P450.

25 20. Sequence according to claim 19, characterized in that the sequence which contains regions having a high content of codons which are poorly suited to yeasts includes the coding region of the sequences ID No. 1 or ID No. 10..

21. Sequence according to claim 19, characterized in that it is one of the sequences ID

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No. 7, ID No. 8, ID No. 9 and ID No. 13.

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22. Chimeric gene which contains a modified DNA sequence according to ~~one of claims 1 to 21~~ and heterologous 5' and 3' regulatory elements which are  
5 able to function in a yeast.

23. Vector for transforming yeasts which contains at least one chimeric gene according to claim 22.

10 24. Process for transforming yeasts using a vector according to claim 23.

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25. Transformed yeast for expressing a protein of interest, characterized in that it contains a chimeric gene according to claim 22.

15 26. Yeast according to claim 25, characterized in that it is selected from among the genera *Saccharomyces*, *Kluyveromyces*, *Hansenula*, *Pichia* and *Yarrowia*, advantageously from the genus *Saccharomyces*, in particular *S. cerevisiae*.

20 27. Process for producing a heterologous protein of interest in a transformed yeast, characterized in that it comprises the steps of:

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25 a) transforming a yeast with a vector ~~according to claim 23~~ which contains a modified DNA sequence according to ~~one of claims 1 to 21~~ and heterologous 5' and 3' regulatory elements which are able to function in a yeast,

b) culturing the transformed yeast, and

c) extracting the protein of interest from

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the yeast culture.

28. Process for transforming a substrate by enzymic catalysis using an enzyme which is expressed in a yeast, which process comprises the steps of

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a) culturing, in the presence of the substrate to be transformed, the yeast which has been transformed with a vector ~~according to claim 23~~ which contains a modified DNA sequence according to one of ~~claims 1 to 21~~ and heterologous 5' and 3' regulatory elements which are able to function in a yeast, and then

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b) recovering the transformed substrate from the yeast culture.

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